Ocular Melanoma – FDA Patient-led Listening Session
Executive Summary

Date: January 27, 2020

Location: Food and Drug Administration, 10903 New Hampshire Ave, Silver Spring, MD

Overview

Ocular melanoma (OM) is a rare form of melanoma that affects the eye. Each year around 2,000 new cases are diagnosed in the United States. Although rare, OM is the second most common form of melanoma and the most common primary eye malignancy in adults. Unlike cutaneous melanoma, ocular melanoma has not been found to be linked to UV exposure and metastasizes in about 50% of all cases (most often to the liver). Although there are treatments proven to control the primary eye tumor, no treatments have been shown to change overall outcomes of the disease in the last 50 plus years.

On January 27, 2020, eleven patients and caregivers along with one ocular melanoma oncologist addressed the Food and Drug Administration (FDA) and provided emotional first-hand accounts of what it is like living and caring for someone with this rare and sometimes fatal disease.

The main topics discussed were:

- Standardization of care, access to care (including clinical trials)
- Impact on quality of life (social and emotional)
- Financial toxicity

The dialogue about patient experience was supplemented with comments from representatives of the broader ocular melanoma community—Melanoma Research Foundation's (MRF) CEO Kyleigh Lipira and Dr. Richard Carvajal, Columbia University Department of Medicine, Director,

Melanoma Service). Approximately 15 members from the FDA attended in person and via teleconference.

Participants:

- Richard Carvajal, Medical Professional/Patient Advocate
- Samantha Buirski, Patient Advocate
- Shea Tyler Buirski, Patient Advocate/Caregiver
- Aaron Davis, Patient Advocate
- Elizabeth Reilly, Patient Advocate
- Sean Hennessey, Patient Advocate/Caregiver
- Sue Colbert, Patient Advocate/Caregiver
- Kristin Nocco, Patient Advocate
- Carla Tressell, Patient Advocate
- Katie Doble, Patient Advocate
- Sara Selig, Patient Advocate/Caregiver, Founder and Director, CURE OM Initiative
- Kyleigh Lipira, CEO, MRF
- Cassie Beisel, Advocacy Officer, MRF
- Lauren Johnston, Program Officer, Rare Melanoma Subtypes, MRF
- Caileigh Lydon, Program Intern, MRF

FDA Divisions Represented:

- **Center for Biologics Evaluation and Research (CBER)**
  - Office of the Center Director
  - Office of Biostatistics and Epidemiology
  - Office of Tissues and Advanced Therapies, Division of Clinical Evaluation & Pharmacology / Toxicology
- **Center for Drug Evaluation and Research (CDER)**
  - Office of New Drugs, Office of Oncologic Diseases, including the Divisions of Oncology Products 2 and 3
  - Office of Biostatistics
  - Rare Disease Program
- **Center for Devices & Radiological Health (CDRH)**
  - Office of Strategic Partnerships and Technology Innovation

- Office of Product Evaluation and Quality; Office of Ophthalmic, Anesthesia, Respiratory, ENT, and Dental Devices

- **Office of the Commissioner (OC)**
  - Office of Clinical Policy & Programs
  - Patient Affairs Staff
  - Office of Orphan Products Development
  - Oncology Center of Excellence

Summary of Topics Discussed

Members from the ocular melanoma community shared their ocular melanoma journey and highlighted the disparities faced when diagnosed and living with this disease.

1. Timely diagnosis is important to people with OM:

OM is a very rare disease and many healthcare providers, ophthalmologists and optometrists are unaware of the signs of OM. Many patients go undiagnosed for months and sometimes years before they get a clear diagnosis and are treated.

- Underdiagnosed and misdiagnosed: People with OM are often diagnosed by using a dilated eye exam. However, more times than not, patients go underdiagnosed or mis diagnosed because of lack of awareness and miseducation on the signs and symptoms of OM. Members of the group expressed their experiences with being misdiagnosed and the lack of standard of care and awareness.

> *"When I first noticed symptoms, I went to the doctor and was misdiagnosed and offered eye drops. It wasn't until I walked into a pole 7 months later, detaching my retina that I was sent to specialist who would diagnose me with ocular melanoma."*

> *"During LASIK, a doctor told me I had a freckle in my eye but there was no need to follow up. I did not go back for an eye exam for five years! At my next exam, I was diagnosed with ocular melanoma."*

- Lack of approved treatment options: Once a diagnosis of OM is made, choice of treatment depends on the location, site of origin within the eye, size of the tumor, as well as patient age, overall health, visual potential and status of the unaffected eye, and patient preference. Currently, there are two main treatment options in the United States to treat primary disease. The first is radiation and the second is removal of the eye. In the United States there are two main forms of radiation:

1. Plaque Brachytherapy (Radiotherapy)- where a thin piece of metal, called a plaque, is sewn onto the tumor. The radioactive seeds in the plaque give off radiation, which aims to kill the cancer. The treatment usually lasts a few days and the plaque is removed at the end of treatment.
2. Proton Beam Radiotherapy – where clips are surgically placed onto the eye at the tumor base and an external beam of radiation is aimed at the tumor, most often through the front of the eye. Treatment is usually finished after 3-5 daily outpatient treatments.

   As mentioned above, if the tumor is too large or not conducive to radiation then enucleation (removal of the eye) is recommended.

   If the melanoma has metastasized, or spread, it can be more difficult to treat. Despite excellent rates of local disease control in the eye, nearly 50% of patients will ultimately develop metastatic disease, with the most common initial site being the liver. Outcomes are exceedingly poor following the development of metastatic disease. Once diagnosed, patients rely heavily on clinical trials or experimental treatments. Members of the group called for new and innovative research, treatments and education around other cancer treatments that could potentially have a positive impact on ocular melanoma

"I had three options, plaque therapy (radiation), laser treatment or enucleation (removing the eye). I opted for laser. But after laser the tumor did not shrink it grew so we then did Plaque, again my tumor grew so eventually I had my eye removed."

"The doctors suggested a more targeted approach. I had a liver embolization procedure to half my liver, which is the only FDA approved treatment for metastatic colon cancer, but due to pain, we were able to get it approved by insurance. Thank God because I believe it saved my life."

- Lack of access to clinical trials: Currently, there are no FDA-approved treatments for this deadly disease once it spreads beyond the eye. There are very few clinical trials available for metastatic disease and patients may not qualify for available trials due to previous treatments. Additionally, because the few clinical trials are often based at only a few centers across the country, access to the trials is challenging due to distance and the time and financial resources it requires to participate. Members of the group talked about the need to expand access to compassionate use "just in time" trials as well as single arm clinical trials which would offer non-randomized trial opportunities.

> *"When something as intense as TIL therapy is on the table and I know my medical center offers it to cutaneous melanoma patients, but not ocular patients, it's so discouraging."*

> *"A recent PET scan showed widespread progression to my liver, lymph nodes, abdomen and multiple soft tissue areas. I am out of treatment options. There are very few clinical trials available for metastatic ocular melanoma."*

> *"By June, my tumors grew so I was transferred to another arm of the trial. In August, additional growth eliminated me from the protocol. Back in Denver, I started a second trial. Severe side effects eliminated me from that trial after just one treatment."*

- Standardization of care: Currently, there are few standards related to obtaining genetic testing of the primary eye tumor. To obtain the genetic information a biopsy of the tumor must be taken and this is not a routine part of care the way biopsies are for other solid tumors. In some cases, patients' tumours have already been treated or removed prior to obtaining a biopsy leaving no option for genetic testing. Additionally, there remain few standards regarding recommendations for surveillance following the treatment of the primary eye tumor. This leaves each patient to educate and advocate for themselves with their healthcare provider. As a result of having few standards of care, patients discussed their difficult experiences with insurance denials for treatments and scans.

> *"My life was at risk because the insurance company was not educated in my type of cancer. I am standing in front of you now, begging you to help us find a standard of care."*

> *"There is a need for standardized follow-up surveillance after primary diagnosis. Some have an MRI; some have an ultrasound, and some have a CT scan. I had an X-ray which, I found out is wrong after metastases was found."*

- Financial toxicity: because the few treatment centres that have experience treating OM are scattered around the country, OM patients often must spend considerable time and money traveling to access specialists and clinical trials. The financial burden does not stop there. Clinical trials are one of the few treatment options available to those with metastatic disease and patients who have the means often pay enormous costs to hire a private patient navigator who can help make sense of the complex system. Members of the group found many common themes in the topics of financial burden listed above.

"Because so much of the treatment was experimental and sometimes off label there were enormous costs to both the treatment and the travel"

"A friend started a GoFundMe account that raised $13k. That money was so beneficial to covering the burden of travel and hotels for treatment and doctor visits. It's gone now and I fear if I end up in another clinical trial out of state again what we will do?"

Quality of life: An ocular melanoma diagnosis can be very stressful for both patients and caregivers. Due to the lack of standardization of care and treatment options as well as the high mortality rate, patients and caregivers often experience high anxiety, depression, loss of hope, frustration, and isolation. Members of the group discussed "scanxiety" and living life from one scan to the next, challenges raising a family with a rare disease and the fear of the unknown when living with a rare cancer.

"After Kenan's treatment failed, she was left to advocate for herself in finding a new clinical trial for her metastatic disease. It concerning, expensive and a shot in the dark"

"Gregg's health took a sudden turn for the worse and the fertility process was stalled only to be picked up by me, alone, after Gregg died. Being widowed at the age of 35 and now raising our young daughter on my own is not the life I would have chosen for myself, for Gregg, and for little Giuliana."

"Quality of life came crashing down after metastasis. What trial do I choose? Do I qualify for a trial? Do I have family support? Who is going to help me finish out the next steps? What about future planning? You cannot 'make plans living between bi-monthly scans."

"Sometimes, my husband and I are living three months at a time – the space between my scans. Other times, when tumor growth happens or I am in treatment, we are living minute by minute. Trying to maintain some semblance of normal, as a young couple who should be starting a family but instead are fighting to stay alive."

Next Steps:

The MRF has followed up with the Center for Devices & Radiological Health (CDRH) and Center for Biologics, Evaluation and Research (CBER) to continue the conversation of ocular melanoma

to address the needs outlined during the OM Patient-Led FDA Listening Session.

Partner Organization:

The MRF worked directly with the FDA to prepare this meeting. The MRF did not pay for the travel or accommodation of the community members that attended this meeting.

Patients Represented:

Out of the eleven participants, two were patients with primary disease, four were patients with metastatic disease, four were caregivers and one was an ocular melanoma specialist.

Disclaimer:

Discussions in FDA Rare Disease Listening Sessions are informal. All opinions, recommendations, and proposals are unofficial and nonbinding on FDA and all other participants. This report reflects the Melanoma Research Foundation's account of the perspectives of patients and caregivers who participated in the Rare Disease Listening Session with the FDA. To the extent possible, the terms used in this summary to describe specific manifestations of [disease or condition], health effects and impacts, and treatment experiences, reflect those of the participants. This report is not meant to be representative of the views and experiences of the entire [disease or condition] patient population or any specific group of individuals or entities. There may be experiences that are not mentioned in this report.